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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,235	03/19/2001	Seishi Kato	GIN-6715CPUS	3254

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/674,235	Applicant(s) KATO ET AL.	
	Examiner Eileen B. O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6* ~~are~~ were subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

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Art Unit: 1646

DETAILED ACTION

1. Claims 1-6 are pending in the instant application.

Election/Restrictions

2. Applicant's election of Group I in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Objections

3.1 Claim 11 is objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

> "Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

The limitations "SEQ ID NO:Y" and "ATCC Deposit No.Z" are each functionally equivalent to a Markush Group. The finite number of express and mutually exclusive embodiments encompassed by these limitations do not share a common utility which is based upon a shared structural feature lacking from the prior art.

3.2 Claims 1-6 are objected to because of the following informalities: claim 2 is objected to for the term "coding for". The art accepted term is "encoding the protein".

3.3 Claims 3 and 4 are also objected to for the term "base sequences". It would clarify the claims if "base" were replaced with "nucleotide" or "nucleic acid".

3.4 Claim 6 is objected to because the word "transformation" should be replaced with the word " transformed" because it is a transformed cell that express the DNA.

3.5 Claim 6 is also objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). It is suggested that the term "producing the protein as claimed in Claim 1" be replaced with "producing a protein comprising the amino acid sequence represented by SEQ ID NO: 1".

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4.1 Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1 and 2 encompass a protein comprising the amino acid sequence of SEQ ID NO: 1 and a DNA encoding the protein, which are compounds which occur in nature. The rejection would be withdrawn if the word "isolated" was inserted before the words "protein" and "DNA".

4.2 Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial utility or a well established utility.

Claims 1-6 are directed to an isolated polypeptide comprising the amino acid sequence shown in SEQ ID NO: 1, which is categorized as a human transmembrane protein. The gene encoding this protein (SEQ ID NO: 10 or 19) is expressed in human liver. The specification asserts many uses for the protein or encoding nucleic acid, however, none of the asserted uses are considered a specific and substantial utility, or a well established, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001, and as discussed below.

The instant specification teaches that Northern blots reveal that the nucleic acid encoding the protein of the instant invention is only expressed in liver, and that the protein is analogous to the rat organic cation transporter. Schoemig et al., database SPTREMBL_19, Aug. 1, 1998, and Grundemann et al., Nature, Vol. 372, pages 549-552, Dec. 8, 1994, disclose a rat polypeptide that is 58.2% identical to amino acids 1-244 of the polypeptide of SEQ ID NO: 1 of the instant application, and is 67.3% identical to amino acids 1-168 (see attached sequence alignment) and Grundemann teaches that the rat organic cation transporter has been found as a membrane protein associated with drug excretion in the kidney. The specification asserts that the protein of the instant invention is its homologue and is considered to possess a similar function and can be utilized for the diagnosis and treatment of diseases that are associated with abnormalities of this protein, and furthermore, this is considered to be associated with a drug excretion, so that the cells expressing this protein can be used as a tool for designing drugs. Also, because the protein is expressed specifically in the liver, a substance prepared so as to possess an affinity with this protein can be applied to the drug delivery system to the liver. It is clear from the instant specification that the human protein described therein is similar in partial sequence structure to

that rat organic cation transporter. However, the protein of Schoemig et al. is 552 amino acids in length, and the protein of Grundemann et al. is 556 amino acids in length, and contains 11 transmembrane domains (See Fig. 2). The protein of the instant invention is only 268 amino acids in length, and contains only two transmembrane domains. Alignment with other similar proteins demonstrates significant differences. For example Suzuki et al., database SPTREMBL_19, Accession No. Q96LX3, Dec. 1, 2001, discloses a human protein that is 55% identical to the protein of the instant invention, but this protein is again 552 amino acids in length. A similar protein from mus musculus, (Strausberg, R., database SPTREMBL_19, Accession No. Q91WJ2, Dec. 1, 2001) is 53.4% identical to the protein of the instant invention, but the mus musculus protein is also 552 amino acids in length. Additionally, all of these proteins contain an additional approximately 108 amino acids inserted between amino acids 168 and 169 of the protein of SEQ ID NO: 1 (see sequence alignments). Given the significant differences in structure between the rat, mouse and the other human protein, and especially in light of the fact that the human protein disclosed by Suzuki et al. is much more similar to the rat and mouse proteins than to the human protein disclosed in the instant application, one of ordinary skill in the art would not conclude that the protein of the instant invention would function in the same manner as the other proteins.

The instant application also describes other uses and methods of the invention, and state that the polypeptide of SEQ ID NO: 1 and/or encoding polynucleotides and/or antibodies to the polypeptide have uses as reagents for tissue or cell type identification, to identify chromosomes or to map related gene positions, to identify individuals from minute biological samples, as molecular weight markers for Southern gels, protein gels or gel filtration columns, probes to

"subtract out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA or anti-proteins antibodies, as an antigen to elicit an immune response, to assay the levels of the polypeptide in biological samples, in vivo imaging, use in assays to screen for molecules that bind to the polypeptide, to recombinantly produce polypeptide, and that the polynucleotides and polypeptide can be used in assays to test for one or more biological activities. However, none of these uses are considered to be specific or substantial utilities for either the nucleic acid, polypeptide or antibodies, because any nucleic acid molecule, polypeptide or antibody can be used in the above ways, and so these are general methods. Any nucleic acid molecule or protein expressed by a tissue or cell type can be used for identification purposes. The assertion that the nucleic acid is useful or to compare with endogenous DNA sequences in patients to identify potential genetic disorders are also not specific and substantial utilities, since no correlation has been made between the nucleic acid and any disease and disorder, so that this is not a specific and substantial utility.

The specification also asserts that the molecules of the instant invention can modulate mammalian characteristics such as body height, weight, eye color and other characteristics listed on page 33, can modulate metabolism, change a mammal's mental or physical state such as tendency for violence and reproductive capacities, or as a food additive or preservative, such as to increase or decrease storage capabilities, fat, lipid or other nutritional components. However, the instant application does not provide any support for any of these asserted utilities.

The specification also teaches that the molecules of the invention may be useful in diagnosing and treating deficiencies or disorders of the immune system, such as hematopoietic

disorders, autoimmune disorders, inflammation or allergic reactions, hyperproliferative disorders, infectious disease, can be used in regeneration of tissues, and may have chemotaxis activity.

There is no nexus between any of the disorders or activities and the molecules of the instant invention. A stated belief that a correlation exists between the nucleic acids or polypeptides and the above diseases and disorders, based on tissue expression alone, is not sufficient guidance to use the claimed polynucleotides or proteins to treat and/or diagnose a particular disease; it merely defines a starting point for further research and experimentation. There is no RFLP polymorphism disclosed for this gene, or any other type of alteration that would result in a change in structure or expression, so the use of the gene as a diagnostic or prognostic marker is conjectural and would not, on the basis of the disclosure, be considered useful by one of skill in the art.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 14
8 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility.

The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "

[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross

what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO: 1, or the gene encoding it, the instant invention is incomplete. In the absence of a knowledge of the any biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. All of the biological activities of a protein need not be known to obtain a patent, but there must be at least one specific and substantial activity, function or use known. This further characterization, however, is part of the act of invention and until it has been undertaken the Applicant's claimed invention is incomplete. Because there is no specific and substantial utility asserted, credibility cannot be assessed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are also rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5 and 6 are indefinite because the claims are improper dependent claims; they recite "...in any of Claim 2 to Claim 4...", so the nucleic acid sequences could be from one, two or all three of the claims. Multiple dependent claims must refer to the claims from which they depend in the alternative only, not inclusively. As written, the vector could comprise a plurality of sequences. It is suggested the claim be rewritten as: "...in any one of Claims 2-4...".

Conclusion

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

JOHN ULM
PRIMARY EXAMINER
GROUP 1600

Patent Examiner